REMARKS

The only issues outstanding in the Office Action mailed October 21, 2003, are the rejections under 35 U.S.C. §112 and §103. Reconsideration of these issues, in view of the following discussion is respectfully requested.

At the outset, it is noted that, under the heading "Final Action", the Office Action discusses 35 U.S.C §112, and concludes, at page 3 of the Office Action, that Applicants' *"should limit their claims to a genus, which finds full support in the specification and should amend the claims to clearly show the criticality of their invention. This means what is unexpected which was not taught, nor suggested by the prior art of record [sic]."* On the one hand, Applicants are somewhat at a loss of how to respond to the assertions at pages 2 and 3 of the Office Action, which are not formulated in a manner of an official objection or rejection referencing a particular section of the statute. On the other hand, as discussed at length below, the specification and claims clearly fully satisfy the requirements of 35 U.S.C §112. In any event, for purposes of clarity, Applicants' discussion below is confined to the rejections of record.

Rejections Under 35 U.S.C. §112

Claims 1-25 have been rejected under 35 U.S.C §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art... to make and/or use the invention." In support of this assertion, the Office Action cites, at pages 4-6, various factors taken from *In re Wands*, 858 F2nd 731, 8 U.S.P.Q 2d 1400 (Fed. Cir 1988), and attempts to show that these factors do not support enablement of the invention. Applicants again respectfully disagree with this analysis.

At the outset, it is noted that, for business reasons and in order to expedite prosecution, (reasons unrelated to patentability). Applicants have amended the present claims so as to focus the invention on the use of one particular gestagen, drospirenone (DRSP). Thus, claim 1 is directed to administration of drospirenone, while claim 3 is directed to administration of drospirenone plus an estrogen, with various estrogens being set forth in claims 4-8. Estradiol is set forth as the estrogen in claim 17, and ethinylestradiol in claim 5 and its dependent claims.

Note also, claims 19 and 20 reciting specific estrogens. The following discussion addresses the specific points raised in this passage of the Office Action.

1. Nature of the Invention:

   See claim 1, and 3, for example. It is submitted that the methods claimed are neither speculative or incredible.

2. State of the Prior Art:

   While it is admitted in the Office Action that PMDD is a distinct clinical entity from PMS, the Office Action characterizes PMDD as a "more severe form of premenstrual symptomology." It is emphasized that PMDD differs from PMS by more than mere symptomology, and attention is again directed to the previously file declaration under 37 C.F.R. §1.132, where it is explained that PMDD is a distinct clinical disorder with a distinct clinical picture, distinguished from PMS not just by severity of symptoms, but by the number and character of symptoms, and also on the basis of response to pharmacological treatment.

3. Predictability in the Art:

   It is again argued in the Office Action, without any stated basis, that predicting which gestagen or estrogen might be useful in the treatment of PMDD is "impossible." Although, not discussed in the present Office Action, Applicants previously argued, and herein maintain, that this is absolutely untrue in view of the relatively simple screening tests known in the art, as well as those given at page 9 of the specification. Moreover, the Office Action has not advanced any basis to doubt that *any* given gestagen or estrogen would be ineffective, other than "general lack of predictability in the pharmaceutical art." While unpredictability may be a factor in evaluating how much experimentation might be necessary, it is quite clear that a disclosure is enabling, even if a considerable amount of experimentation is needed, if such experimentation is merely routine. See *Ex parte* Forman, 230 U.S.P.Q. 546 (BPAI 1986) and *In re Wands*, cited in the Office Action. In short, predicting whether a given combination of compounds would work in treatment of PMDD is not "impossible", in view of the screening protocol

given in the specification and known in the art. It is submitted that, in view of the routineness of this screening protocol, such experimentation is not *undue*. Moreover, it is noted that the evaluation of undue experimentation is of a *single compound*; the fact that even a vast number of compounds might need to be tested is not material to undue experimentation, where the test of *each* compound itself is routine. See *In re Colianni*, 561 F.2d 220, 195 USPQ 150 (CCPA 1977). Thus, predicting whether a given gestagen or gestagen/estrogen contradiction is fully routine.

4. Working Examples:

While the Office Action apparently dislikes the working example, which demonstrates "significant improvement" in various symptoms based on the combination of a gestagen and estrogen, it is submitted that the choice of terms used in the examples is not a basis for objection. Because the symptoms are subjective, subjective description must be used in evaluating them. The examples clearly show an improvement and are thus probative. The Office Action should not substitute its judgment for that of the ordinary skilled artisan, for whom such terminology is acceptable.

5. Breadth of the Claims:

With respect to the breadth of the claims, attention is again directed to claims 1 and 3. Moreover, breadth itself is absolutely not determinative of enablement, see *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q 367 (CCPA 1971). The *Marzocchi* Court held that the first paragraph of 35 U.S.C §112 requires only *objective* enablement, and such objective enablement is supplied even if broad terms are used, where specification teaches the manner and process of making and using the invention. Such objective enablement *must*, according to the Court, be taken as sufficient under 35 U.S.C §112 unless there is reason to doubt the truth of such statements. Thus, where - as here - the specification teaches that the entirety of the material claimed is operative, the *breadth* of the claims is not a factor in determining enablement.

6. Quantity of Experimentation:

It is additionally noted that experimentation, even if necessitating testing a large number of compounds, is not undue in view of the routine nature of the screening. The test of whether experimentation is "undue" is on a compound by compound basis; the fact that a large number of compounds must be tested is immaterial so long as each test is routine. See *In re Colliani, supra*, which held that determination of operability of a claim is on an embodiment-by-embodiment basis. The fact that any large number of embodiments must be considered is *not* relevant to undue experimentation if it is not undue to determine operability of each single embodiment one at a time. Because one of ordinary skill can determine whether a given gestagen or estrogen combination will work in accordance with the protocol in the specification, and as known in the art, any experimentation is not undue.

In short, the "*Wands*" factors clearly show that the present method claims are fully enabled.

In the prior Reply, as further evidence of enablement of the claims, Applicants cited Freeman et al., J. Women's Health Gend. Based Med. 10(6) 2001, pp. 561-9. In this article, the authors demonstrate the beneficial effect of drospirenone and an estrogen on PMDD. (The article is supplied with the IDS filed previously; the article is post-published and does not constitute prior art. One of the authors is employed by the U.S. subsidiary of the assignee of the present application.) This article, while post-published, clearly supports Applicants' position that the presently claimed process is effective. The use for such purpose of material published after applicants' filing date is, of course, permissible. See *EnzoBiochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1998).

As even further evidence of the operability and thus enablement of the present invention, Applicants' submit herewith a Declaration under 37 C.F.R.§1.132, providing unequivocable evidence of efficacy of the present invention. This evidence clearly rebuts any reasons or evidence expressed by the PTO casting doubt upon Applicants' objective enablement.

In short, withdrawal of the rejection under 35 U.S.C §112 is appropriate and is respectfully requested.

Rejection Under 35 U.S.C. §103

Claims 1-15 remain rejected under 35 U.S.C §103 over Dennertein, et al. (British Medical Journal 200 (1617-1621) and Gullberg. Reconsideration of this rejection is again respectfully requested.

Claims 1-23 have also been rejected under 35 U.S.C §103 over Harvard, Rev. Psychiatr., vol. 2, no. 5 (1995), pages 233-245. Reconsideration of each of these rejections is respectfully requested.

All the cited references deal with various gestagens and/or estrogens for use in treating PMS. The rationale underlining these rejections, simply stated, is that "some of the same symptoms exist in PMS as in PMDD, and thus drugs which show promise for the treatment of PMS are obvious to treat PMDD." At best, such drugs might be *obvious to try*, but this does not rise to the level of obviousness required to support a rejection under 35 U.S.C §103. See, e.g., *Merck v. Biocraft*, 10 USPQ2d, 1843 (Fed Cir 1989). As discussed at length in the prior declaration, It is understood and recognized by researchers and practitioners in the field of obstetrics and gynecology that PMS (premenstrual syndrome) and PMDD (premenstrual dysphoric disorder), while sharing some of the same signs and symptoms, have important and distinguishable differences.

The differences between PMS and PMDD are differences of kind, not mere degree. For example, PMDD usually comprises extremely distressing emotional and behavioral symptoms including irritability, dysphoria, tension, and mood liability which may be accompanied by physical complaints. Symptoms appear 3 to 10 days *prior* to the onset of menstrual bleeding and remits *after* menses. The symptoms of PMDD are severe enough to impair social and occupational functioning. Approximately 3-8% of women of reproductive age are affected (Steiner, M. and Born, L. (2000)*Inter. Clin. Psychopharmacology*; 15 (suppl 3): S15-S17). Thus, PMDD has a distinct clinical picture wherein the symptoms include irritability, anger, and tension and the physical symptoms which include breast tenderness and bloating are *unique*. Also, gonadal hormone suppression has been used to relieve symptoms and serotonergic

antidepressants can be used for treatment.

By contrast, PMS affects approximately 75% of women of reproductive age and the symptoms appear in the *luteal* phase and *cease* with menses. (The difference in onset and remission alone are submitted to constitute such considerable differences so as to prohibit any inference of motivation to employ a treatment for one indication in the other.) There are neither functional impairments nor specific charting requirements. Furthermore, typical treatment for PMS patients consists of a non-pharmacologic approach including conservative modalities such as lifestyle changes, stress management, diet, exercise, nutritional supplements, and cognitive/behavioral therapy. Attention is again directed to the *clinical differences* between these indications, set forth at page 3 of the prior declaration. It is, thus, not simply a matter of severity of symptoms; clearly, the indications possess different functional nature. Thus, it is emphasized again, that one of ordinary skill in the art would *not* automatically find it obvious that a treatment which might be employed for PMS, should also be employed for PMDD. As such, one of ordinary skill in the art, at best, might find it "obvious to try" such a treatment, but such does not rise to the level of motivation required under the statue. Thus, it is submitted that, on this basis alone, the references do not support a rejection under 35 U.S.C §103.

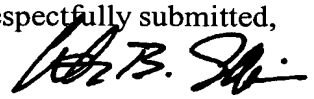
Moreover, neither reference employed in the rejection teaches the use of Drospirenone as a gestagen. It is submitted that there has been established absolutely no motivation not only to move from treatment of PMS with PMDD, but to do so with a gestagen not employed or suggested in Dennertein or Gullberg.

Thus, it is respectfully maintained that the claims are not obvious under 35 U.S.C §103 and withdrawal of the rejection is again respectfully requested.

The claims of the application are submitted to be in condition for allowance. However, if the Examiner has any questions or comments, she is cordially invited to telephone the undersigned at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Harry B. Shubin (Reg. No. 32,004)
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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